

## Comorbidity of Adult Attention Deficit and Hyperactivity Disorder in Bipolar and Unipolar Patients

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### ABSTRACT

**Introduction:** The co-occurrence of attention deficit hyperactivity disorder (ADHD) in affective disorder patients is considerably high. The aims of the present study were to search for the frequency and impact of ADHD co-occurrence on the clinical features of affective disorders and to examine the relationship between the dominant affective temperaments and ADHD.

**Methods:** In total, 100 patients with bipolar disorder (BD), 100 patients with major depressive disorder (MDD), and 100 healthy controls (HC) were included. All diagnoses were assigned according to DSM-IV-TR criteria. The Adult Attention Deficit and Hyperactivity Self-Report Scale (ASRS); Wender Utah Rating Scale (WURS); and Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A) were applied to all participants.

**Results:** The percentage of BD patients meeting the criteria for a diagnosis of current ADHD was 48% compared with the percentage of MDD patients and HCC subjects, i.e., 25% and 12%, respectively. ADHD was significantly more frequent in bipolar adults than in not

only HC but also depressive patients. In the BD group, patients with a comorbid ADHD diagnosis had significantly more suicidal history than those without ADHD. The scores of the temperament traits, namely depressive, cyclothymic, irritable, and anxious, were significantly higher in subjects with ADHD in all groups, including in HC.

**Conclusion:** The most important findings of the present study were the observations that (1) the frequency of ADHD is considerably high among bipolar patients; (2) the frequency of suicide attempts is high in the bipolar patient group with comorbid ADHD; and (3) depressive, cyclothymic, irritable, and anxious temperaments are significantly associated with ADHD comorbidity in bipolar and depressive patients as well as in HC. The high comorbidity and chronic course of ADHD and its possible negative influence on the course of both disorders increase the importance of screening for adult ADHD.

**Keywords:** Attention deficit hyperactivity disorder; affective disorder; bipolar; depression; temperament.

### INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is characterized by persistent and developmentally inappropriate levels of impulsivity, attention problems, and hyperactivity. Mood instability, impairments in social and family relationships, and school and work performance are the other features of the disorder (1,2). The prevalence of the disorder is estimated to affect approximately 3%–4% of the adult population (3,4). The clinical presentation of ADHD in adults includes fewer externalizing symptoms and a different profile of psychiatric comorbidities (2,5).

In adults with major depressive disorder (MDD), the prevalence of co-occurring ADHD was 5%–12% (6,7,8). Subjects suffering from both disorders showed a poorer prognosis with more severe symptoms (9,10). ADHD is frequently observed in adults with bipolar disorder (BD), with comorbidity rates ranging from 9.5% to 21% (3,6,11). Similarly, bipolar patients with ADHD comorbidity are reported to have an earlier disease onset, more affective episodes, more suicide attempts, and a greater likelihood of suffering from anxiety disorders (11,12).

Despite the significant comorbidity between ADHD and affective disorders, there are limited data for investigating this relationship in terms of temperamental features and clinical characteristics. To date, existing studies mainly focus on children and young adults (13,14). Several studies have found that cyclothymic temperament is more frequent in patients with ADHD (15). Exploring temperamental traits may contribute to our understanding of the co-occurrence of ADHD and affective disorders.

Thus, the aims of the present study were (1) to assess adults in remission with BD and MDD for ADHD and investigate the impact of ADHD co-occurrence on the clinical features of affective disorders and (2) to examine the relationship between the dominant affective temperaments and ADHD.

### METHODS

The study protocol was approved by the institutional review board of Gaziosmanpaşa University School of Medicine, and written informed consent was obtained from each participant prior to study enrollment. All patients, who consecutively applied to Gaziosmanpaşa University Research and Training Hospital between June and November 2012 and who were diagnosed with MDD or BD, were screened for eligibility for the study.



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and 100 patients were included in each group. Affective disorders diagnoses were assigned using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (16). Inclusion criteria were as follows: age between 18 and 65 years, DSM-IV-TR diagnosis of MDD or BD in remission for at least 8 weeks, scores of 12 or below on the Hamilton Depression Rating Scale, and scores of 5 or below on the Young Mania Rating Scale. Exclusion criteria were as follows: psychotic features, substance/alcohol abuse in the last month, organic brain syndromes, any clinically significant medical condition that might have a psychiatric manifestation, diagnosis of mental retardation, cognitive impairment, or an unwillingness or inability to provide informed consent or to comply with assessment. ADHD diagnosis was based on DSM-IV-TR criteria for any of the three subtypes of ADHD (combined, predominantly inattentive, and predominantly hyperactive/impulsive).

One hundred healthy controls (HC) were randomly recruited among the mentally ill patients' relatives and from healthcare professionals. Exclusion criteria for the control group included lifetime history of brain trauma, neurological or major psychiatric illnesses, and psychopharmacological or psychotherapeutic treatments.

The following tools were applied in order to assess adult ADHD features and the temperamental traits:

**The Adult Attention Deficit and Hyperactivity Self-Report Scale (ASRS)**, an 18-item self-rating scale based on DSM-IV criteria for ADHD, was used to assess the severity of current ADHD. The scale has two sub-scales, namely attention deficit and hyperactivity-impulsivity. Turkish validity and reliability studies were conducted by Dogan et al. (17).

**The Wender Utah Rating Scale (WURS)**, a 25-item self-administered instrument, retrospectively measures ADHD-relevant childhood behaviors and symptoms (18). It has 5 sub-scales, including attention deficit, irritability, depression, impulsivity, and school problems. Turkish validity and reliability studies were carried out by Oncu et al. (19).

**The Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire/TEMPS-A** (Turkish Form of Memphis, Pisa, Paris, and San Diego Temperament Evaluation Questionnaire/MPPS-MD) is a scale developed by Akiskal in order to evaluate dominant affective temperament (20). The questionnaire includes 100 items organized to determine depressive, hyperthymic, aggressive, cyclothymic, and anxious temperaments. The validity and reliability studies of the Turkish form were carried out by Vahip et al. (21).

### Statistical Analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS Inc.; Chicago, IL, USA) 16.0 for Windows program.

In our study, the distribution of participant in the groups was homogeneous; the arithmetic mean, standard deviation, and standard error values related to the distribution of continuous data determined through measurement are presented. The frequency and percentage distribution of the discrete (qualitative) data are also presented.

In our study, the chi-square test was used for analyzing the relation between the discrete (qualitative) data. While the t-test for independent samples was used in comparison of the differences between the variables with ( $k=2$ ) size number determined through measurement. When the size number  $k$  was  $\geq 3$ , the differences between the averages were analyzed through One-Way Analysis of Variance, and the groups were bilaterally compared through the Tukey-HSD as one of the post hoc tests when differences were noticed between the groups according to the variance analysis results.

Finally, the levels of relationship between the variables determined in the measurements were analyzed through Pearson Correlation Coefficient as one of the Simple Correlation Analysis methods. In our study, the level of  $p \leq 0.05$  was accepted as significant.

### RESULTS

The groups consisted of 100 BD and 100 MDD patients, in remission at the time of the study, as well as 100 HC subjects. All the groups were similar with respect to age, gender, and level of education ( $F=0.878$ ,  $p=0.417$ ;  $\chi^2=0.000$ ,  $p=1.000$ ;  $F=1.192$ ,  $p=0.305$ ).

The percentage of BD patients meeting criteria for a diagnosis of current ADHD was 48% ( $n=48$ ) compared to the 25% ( $n=25$ ) of MDD patients and the 12% ( $n=12$ ) of HC subjects. ADHD occurrence was significantly higher in the BD group compared to both the MDD group ( $p=0.0312$ ) and the HC group ( $p=0.0119$ ). No significant difference was observed between the MDD patient group and the HC subjects ( $p=0.314$ ). In the BD group with ADHD, 22 patients fulfilled DSM-IV criteria for the predominantly inattentive subtype, 10 patients for the predominantly hyperactive/impulsive subtype, and 16 patients for the combined subtype. In the MDD group with ADHD, 7 patients were diagnosed with the predominantly inattentive subtype, 5 with the predominantly hyperactive/impulsive subtype, and 13 with the combined subtype. In the HC group with ADHD, 3 patients were diagnosed with the predominantly inattentive subtype, 2 with the predominantly hyperactive/impulsive subtype, and 7 with the combined subtype.

The clinical features of the BD and MDD patient groups are presented in Table 1. In the BD group, patients with a comorbid ADHD diagnosis had significantly more suicidal history than those without a comorbid diagnosis of ADHD. No significant differences were observed with respect to the duration of disease, age at onset, bipolar type, psychotic, or seasonal features. In the MDD group, patients with and without ADHD comorbidity did not show any significant difference in terms of any of the clinical features.

Other comorbid Axis I Disorders were: nicotine dependence ( $n=25$ , 25%), obsessive compulsive disorder ( $n=5$ , 5%), social phobia ( $n=4$ , 4%), generalized anxiety disorder ( $n=3$ , 3%) in the BD group, and nicotine dependence ( $n=25$ , 25%), generalized anxiety disorder ( $n=5$ , 5%), obsessive compulsive disorder ( $n=2$ , 2%), and panic disorder ( $n=2$ , 2%) in the MDD group.

The results from the ADHD assessment scales are displayed in Table 2. The overall differences in the total scores of both scales between the HC and each patient group were statistically significant. The ASRS and WURS total scores were significantly higher in patients with affective disorders compared to the HC. When the two patient groups were compared, the BD patients had higher scores than the MDD patients; yet, the difference did not reach significance.

A comparison of ASRS and WURS between the bipolar and unipolar patients with and without current ADHD diagnosis is presented in Table 3. The total and the subscale scores of both scales were significantly higher in patients with a comorbid diagnosis of ADHD in both affective disorder groups.

The relationships between the temperament traits of all the groups with and without ADHD are presented in Table 4. The scores of four traits, namely depressive, cyclothymic, irritable, and anxious, were significantly higher in subjects with ADHD in all the groups. Interestingly, the scores of the hyperthymic trait did not show any significant difference between subjects with and without co-occurring ADHD in all three groups.

**Table 1.** Comparison of the patient groups in terms of clinical features

	<b>BD with ADHD n=48 (48%)</b>	<b>BD without ADHD n=52 (52%)</b>		<b>p</b>	<b>MDD with ADHD n=25 (25%)</b>	<b>MDD without ADHD n=75 (75%)</b>		<b>p</b>
BD-I	39 (39%)	48 (48%)	$\chi^2=2.693$	0.100	-	-		
BD-II	9 (9%)	4 (4%)	$\chi^2=2.671$	0.102	-	-		
Duration of disease	13.04±9.08	13.36±10.30	t=0.166	0.868	7.32±5.77	5.01±4.83	t=1.965	0.052
Age at onset	26.52±27.15	27.15±10.20	t=0.307	0.759	31.00±8.95	32.69±10.86	t=0.703	0.484
Psychotic features	26 (26%)	31 (31%)	$\chi^2=0.302$	0.582	3 (3%)	7 (7%)	$\chi^2=0.148$	0.708
Seasonal features	18 (18%)	21 (21%)	$\chi^2=0.087$	0.768	1 (1%)	5 (5%)	$\chi^2=0.236$	1.000
Suicide attempts	17 (17%)	9 (9%)	$\chi^2=4.254$	0.039	7 (7%)	8 (8%)	$\chi^2=4.18$	0.051

BD: bipolar disorder; ADHD: attention deficit hyperactivity disorder; MDD: major depressive disorder; BD-I: bipolar disorder I; BD-II: bipolar disorder II.

**Table 2.** Comparison of the ADHD assessment scales of all the groups

	<b>BD (1)</b>	<b>MDD (2)</b>	<b>HC (3)</b>	<b>F</b>	<b>p</b>	<b>p (Tukey HSD)</b>
ASRS, total	29.97±11.83	25.84±11.41	20.29±11.25	11.878	0.0001	p (1-2)=0.391 p (1-3)=0.001 p (2-3)=0.002
ASRS, attention deficit	14.67±7.04	13.18±6.34	9.92±6.13	13.889	0.0001	p (1-2)=0.240 p (1-3)=0.0001 p (2-3)=0.001
ASRS, hyperactivity-impulsivity	13.30±6.39	12.66±6.08	10.47±6.04	5.772	0.003	p (1-2)=0.744 p (1-3)=0.004 p (2-3)=0.034
WURS, total	26.19±17.18	23.85±17.97	16.73±11.11	9.814	0.0001	p (1-2)=0.545 p (1-3)=0.0001 p (2-3)=0.004
WURS, attention deficit	6.04±3.69	5.84±4.05	4.75±3.26	3.549	0.030	p (1-2)=0.922 p (1-3)=0.037 p (2-3)=0.093
WURS, irritability	7.89±5.77	7.00±6.93	4.21±3.66	11.657	0.0001	p (1-2)=0.503 p (1-3)=0.001 p (2-3)=0.002
WURS, depression	6.26±5.00	5.80±4.78	3.23±3.19	13.741	0.0001	p (1-2)=0.741 p (1-3)=0.0001 p (2-3)=0.0001
WURS, impulsivity	3.16±3.53	3.12±3.21	2.76±2.59	0.492	0.612	p (1-2)=0.996 p (1-3)=0.640 p (2-3)=0.697
WURS, school problems	2.76±2.93	2.00±2.35	1.78±2.07	4.297	0.014	p (1-2)=0.079 p (1-3)=0.015 p (2-3)=0.805

ADHD: Attention Deficit Hyperactivity Disorder; ASRS: Adult Attention Deficit and Hyperactivity Self-Report Scale; WURS: Wender Utah Rating Scale; BD: Bipolar Disorder; MDD: Major Depressive Disorder; HC: Healthy Control.

## DISCUSSION

In the present study, ADHD co-occurrence was 48% in bipolar and 25% in depressive adult patients. ADHD was significantly more frequent in bipolar adults than in not only HC but also depressive patients. No significant difference was observed between the depressive patient group

and HC. A review of the literature indicates that the lifetime occurrence of ADHD among affective disorder patients is high. The frequency of ADHD changes between 9% and 94% in bipolar patients and up to 38% in depressive patients (22,23,24,25). The discrepancy among the findings may arise from the methodological differences and the sampling techniques. The

**Table 3.** Comparison of the ADHD assessment scales of the patient groups with and without ADHD

	<b>BD with ADHD n=48 (48%)</b>	<b>BD without ADHD n=52 (52%)</b>	<b>t</b>	<b>p</b>	<b>MDD with ADHD n=25 (25%)</b>	<b>MDD without ADHD n=75 (75%)</b>	<b>t</b>	<b>p</b>
ASRS total	37.18±7.96	19.46±7.72	11.297	0.0001	41.12±6.12	20.74±7.55	12.197	0.0001
ASRS, attention deficit	19.75±5.66	9.98±4.48	9.598	0.0001	21.2±4.69	10.53±4.27	10.463	0.0001
ASRS, hyperactivity-impulsivity	17.43±5.74	9.48±4.22	7.930	0.0001	20.00±4.51	10.21±4.31	9.700	0.0001
WURS, total	35.43±17.82	17.65±11.22	6.020	0.0001	39.24±20.59	18.72±13.71	5.665	0.0001
WURS, attention deficit	7.66±3.81	4.53±2.87	4.653	0.0001	8.32±4.34	5.01±3.61	3.758	0.0001
WURS, irritability	10.60±5.63	5.38±4.69	5.045	0.0001	12.84±8.17	5.05±5.22	5.542	0.0001
WURS, depression	4.81±4.17	1.63±1.81	5.007	0.0001	5.68±3.74	2.26±2.51	5.160	0.0001
WURS, impulsivity	8.56±5.46	4.13±3.40	4.904	0.0001	8.96±5.60	4.74±3.99	4.108	0.0001
WURS, school problems	3.64±3.39	1.94±2.17	3.013	0.003	3.36±3.17	1.54±1.81	3.525	0.001

BD: bipolar disorder; ADHD: Attention Deficit Hyperactivity Disorder; MDD: Major Depressive Disorder; ASRS: Adult Attention Deficit and Hyperactivity Self-Report Scale; WURS: Wender Utah Rating Scale.

**Table 4.** Comparison of TEMPS-A of all the groups with and without ADHD

	<b>BD with ADHD n=48 (48%)</b>	<b>BD without ADHD n=52 (52%)</b>	<b>p</b>	<b>MDD with ADHD n=25 (25%)</b>	<b>MDD without ADHD n=75 (75%)</b>	<b>p</b>	<b>HC with ADHD n=12 (12%)</b>	<b>HC without ADHD n=88 (88%)</b>	<b>p</b>
TEMPS-A, depressive	9.66±3.82	6.13±2.99	0.0001	11.04±3.38	7.05±3.63	0.0001	8.25±3.62	5.10±3.22	0.002
TEMPS-A, cyclothymic	13.04±4.67	8.03±4.84	0.0001	13.08±3.23	7.69±4.67	0.0001	10.25±3.59	5.81±4.30	0.001
TEMPS-A, hyperthymic	9.33±5.07	9.90±3.63	0.517	8.52±4.70	8.14±4.53	0.725	7.83±5.58	8.27±5.29	0.789
TEMPS-A, irritable	7.81±4.66	4.07±3.60	0.0001	8.84±3.47	4.13±3.91	0.0001	8.00±4.19	3.75±3.19	0.0001
TEMPS-A, anxious	11.70±6.54	5.86±4.72	0.0001	14.92±5.50	8.73±6.06	0.0001	12.00±6.60	5.82±4.37	0.0001

BD: bipolar disorder; ADHD: Attention Deficit Hyperactivity Disorder; MDD: Major Depressive Disorder; HC: healthy control; TEMPS-A: Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire.

patients in our sample were in remission for at least the last 8 weeks, which made it possible for us to state that adult ADHD was not an overlap at the symptom level in affective disorder. Rather, it may possibly result from the common neurobiological mechanisms and genetic factors (2,26).

In our study, ADHD assessment scales were significantly higher in bipolar and depressive adults than in HC. As expected, in each affective group, the total and all subscale scores were significantly higher in adults with ADHD co-occurrence. While several recent studies have reported significantly higher scores on WURS and ASRS in bipolar patients than in depressive patients and HC, others have observed high scores in both bipolar and depressive patient groups (6,7,26,27,28,29). Possible explanations for our similar findings in both affective groups may lie in the fact that all our patients were under treatment and were evaluated with self-rated scales.

One of the assumptions is that ADHD in childhood could be a sign of an early-onset BD (4,8,11,28,30). In our study, the age at onset of bipolar disease was similar in patients with (26.52±10.37) and without (27.15±10.20) ADHD comorbidity. Nierenberg et al. (11) stated that the onset age of BD was particularly important, and that BD and ADHD association was a sub-group starting during early childhood, and therefore should be differentiated from BD with an onset at an adult age. On the other hand, there are studies that did not support this assumption and found a similar disease onset age between bipolar groups with and without ADHD comorbidity (6,31,32), while others have observed a

significantly earlier disease onset in the presence of ADHD comorbidity (15,22,28). McIntyre et al. (7) revealed in their study that lifelong ADHD comorbidity in both MDD and BD was associated with an early onset of mood disorder. Our results did not support the view that BD patients with adult ADHD had an earlier disease onset. Further research with longitudinal follow-up from childhood might be able to clear up some of these assumptions.

Compared to patients without ADHD comorbidity, in the bipolar patient group with comorbid ADHD, we observed a significantly high frequency of suicide attempts. A review of the literature here again indicated contradictory findings. While there were studies observing no difference between bipolar patients with and without ADHD comorbidity in terms of suicide attempt history (15,23), others reported significantly more suicide attempts in the group with comorbidity (11,30,33,34,35). Since the patients diagnosed with both diseases experience impulsivity, difficulty in controlling themselves, and negative life events more frequently, suicide attempts may be expected (36).

Another remarkable finding of our study was that although it did not reach statistical significance and stayed at a value slightly above the limit ( $p=0.051$ ), the history of suicide attempts was more frequent in MDD patients with ADHD comorbidity. There have been studies reporting that the risk for suicide, which is already high due to the leading symptoms in depressive patients, such as depressive mood and hopelessness, might be expected to increase in the presence of ADHD comorbidity (37).

We also examined the psychotic and seasonal features and found no significant relationship with ADHD comorbidity in both BD and MDD patient groups. In accordance with our findings, one study reported that ADHD comorbidity in BD was not associated with psychotic or seasonal features (23). Regarding the bipolar type, there have been different viewpoints in the articles reporting that ADHD comorbidity was more frequent (5), less frequent (11), or at a similar frequency (6,28) in BD type 2. Our findings did not support any difference between bipolar type 1 or 2 in terms of ADHD comorbidity, which at this point may be questioned since the number of BD type 2 patients was relatively small.

Exploring the temperamental dimensions may help our understanding of the etiology of ADHD and affective disorders co-occurrence. In fact, temperament is an innate, genetic biological-origin feeling, thought and behavior pattern, which typically manifests after childhood and continues throughout life (6,38,39). There have been a small number of studies investigating the temperament in patient groups diagnosed with ADHD, with the majority of those carried out on pediatric patients (40,41,42). In their study, West et al. (43) reported that children diagnosed with both BD and ADHD were difficult even when they were 0–18 months old, e.g., they slept harder, cried more, break-up anxiety was more specific. In one study, adult ADHD patients were evaluated with the Temperament and Character Inventory and displayed higher novelty seeking, harm avoidance, self-transcendence and lower reward dependence, persistence, self-directedness, and cooperativeness (44). Our study showed that on TEMPS-A, four traits, namely depressive, cyclothymic, irritable, and anxious, were significantly higher in subjects with ADHD in all groups, including HC. Interestingly, the scores of the hyperthymic trait did not show any significance between subjects with and without co-occurring ADHD in all three groups. Two studies investigated the temperament traits of patients diagnosed with ADHD using the TEMPS-A scale and found that cyclothymic temperament was at a significantly higher level in patients with ADHD (15,45).

The present study has some limitations. First, it was not a follow-up trial, rather a cross-sectional study. Therefore, our assumptions were limited since this method was inadequate in terms of analyzing the effect of comorbidity in a disease group upon progress of the disease. In all three study groups, a valid and reliable structured clinical interview scale adapted into Turkish was used in order to make a diagnosis. Since the field studies of DSM-IV were only carried out upon children, large-scale field studies are still needed for ADHD criteria in adults. In some adult patients, although DSM criteria were administered specifically, establishing ADHD diagnosis in an adult patient benefiting from the available diagnosis criteria is hard. In most studies, only BD is investigated in terms of ADHD co-occurrence; in our study, however, major depressive patients were compared as well as control subjects. The relatively small size of the sample was another limitation and thus larger studies are needed in order to make better comparisons.

The present study's most important findings are the observations that first, the frequency of ADHD is considerably high among bipolar patients; second, in the bipolar patient group with comorbid ADHD, the frequency of suicide attempts is high; and third, depressive, cyclothymic, irritable, and anxious temperaments were significantly associated with ADHD comorbidity in bipolar and depressive patients, as well as in HC. The high comorbidity and the chronic course of ADHD and its possible negative influence on the course of both disorders increase the importance of screening for ADHD, even during the adulthood period.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Gaziosmanpaşa University School of Medicine.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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